PRODUCT MONOGRAPH

BACTROBAN®

(mupirocin)

Ointment 2%
For Dermatologic Use

TOPICAL ANTIBIOTIC

GlaxoSmithKline Inc.
7333 Mississauga Road North
Mississauga, Ontario
L5N 6L4

DATE OF PREPARATION:
2001.07.05

Control No.: 072194

NAME OF DRUG

BACTROBAN®

(mupirocin)

THERAPEUTIC CLASSIFICATION

Topical Antibiotic

ACTION

Mupirocin exerts a bactericidal action against sensitive organisms by inhibiting bacterial protein synthesis. It reversibly and specifically binds to bacterial isoleucyl transfer-RNA synthetase.

INDICATIONS AND CLINICAL USES

BACTROBAN (mupirocin) is considered appropriate for the topical treatment of the following when caused by sensitive strains of staphylococcus and streptococcus species:

- impetigo
- superficially infected dermatoses
- lesions which are moist and weeping

For abrasions, minor cuts and wounds, the use of BACTROBAN may prevent the development of infections by sensitive Gram-positive organisms.

No cross-resistance has been shown between mupirocin and other commonly used antibiotics

CONTRAINDICATIONS

BACTROBAN (mupirocin) is contraindicated in patients with hypersensitivity to mupirocin or to other ointments containing polyethylene glycols.

WARNINGS

This mupirocin ointment formulation is not suitable for ophthalmic or intranasal use or use in conjunction with cannulae.

Polyethylene glycol can be absorbed from open wounds and damaged skin. It is excreted by the kidneys. As with other polyethylene glycol based ointments, BACTROBAN should not be used in conditions where absorption of large quantities of polyethylene glycol is possible, especially if there is evidence of moderate or severe renal impairment.

In the rare event of a possible sensitization reaction or severe local irritation occurring with the use of BACTROBAN, treatment should be discontinued and appropriate alternative therapy for the infection instituted.

PRECAUTIONS

Use of topical antibiotics occasionally allows overgrowth of non-susceptible organisms. If this occurs, or irritation or sensitization develop, treatment should be discontinued and appropriate therapy instituted.

Use in Pregnancy

The safety of BACTROBAN (mupirocin) in the treatment of infections during pregnancy has not been established. If administration to pregnant patients is considered necessary, its potential benefits should be weighed against the possible hazards to the fetus.

Use in Nursing Mothers

Caution should be exercised when BACTROBAN ointment is administered to nursing mothers. If a cracked nipple is to be treated, lactation from the affected breast should be maintained by manual expression until the end of treatment. During this time, milk from the affected breast should be discarded.

ADVERSE REACTIONS

The following local adverse reactions have been reported during therapy with BACTROBAN (mupirocin): itching, burning, erythema, stinging, and dryness. It was not usually necessary to discontinue therapy due to these adverse reactions. Systemic allergic reactions have been reported with Bactroban ointment. Cutaneous sensitization reactions to mupirocin or the ointment base have been reported rarely.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

Overdosage has not been known to occur during topical therapy with BACTROBAN (mupirocin) ointment.

DOSAGE AND ADMINISTRATION

A small amount of BACTROBAN ointment should be applied to the affected area three times daily for up to 10 days, depending on the response. The area treated may be covered with a gauze dressing if desired.

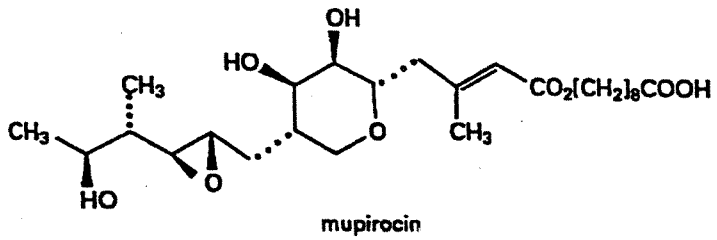
PHARMACEUTICAL INFORMATION

Chemistry:

Trade Name: BACTROBAN

Proper Name: mupirocin

Chemical Structure:



mupirocin

Molecular Formula: $C_{26}H_{44}O_9$

Molecular Weight: 500.6

Chemical Name: 9-{4-[5S-(2S,3S-epoxy-5S-hydroxy-4S-methylhexyl)-3R,4R-dihydroxytetra-hydropyran-2S-y1]-3-methylbut-2(E)- enoyloxy}-nonanoic acid

Description: Mupirocin is a white to off-white solid

Composition: Each gram of BACTROBAN ointment 2% contains 20 mg mupirocin in a bland water-soluble ointment base consisting of polyethylene glycol 400 and polyethylene glycol 3350 (polyethylene glycol ointment U.S.P.)

Storage: BACTROBAN (mupirocin) should be stored at room temperature.

DOSAGE FORMS

BACTROBAN (mupirocin) ointment 2% is available in 15 gram and 30 gram tubes.

MICROBIOLOGY

BACTROBAN (mupirocin) is active against those micro-organisms responsible for the majority of skin infections. It is particularly active against staphylococci, including methicillin-resistant strains. It is also active against many Gram-negative bacteria as a result of the high concentrations achieved after topical administration. Most strains of Morganella morganii, Serratia marcescens and Pseudomonas aeruginosa are resistant. It is not active against most anaerobic bacteria, mycobacteria, mycoplasma, chlamydia, yeast, and fungi. The in vitro activity of BACTROBAN against strains of various organisms is presented in Table 1.

Table 1 **IN VITRO ACTIVITY OF BACTROBAN**

Laboratory Species	MIC (μg/ml)
AEROBIC GRAM-POSITIVE	
Staphylococcus	
S. epidermidis	0.5
S. haemolyticus	0.5
S. hominis	0.5
S. saprophyticus	0.12
S. aureus	0.25
Streptococcus	
S. pyogenes	0.12
S. species	0.12
S. species	0.25
S. agalactiae	0.5
S. mutans	0.5
S. sanguis	1.0
S. faecium	32
S. faecalis	64
Corynebacterium	
C. hofmannii	64
C. xerosis	>128
C. Group	>128
Bacillus subtilis	0.12
Micrococcus luteus	>128
AEROBIC GRAM-NEGATIVE	
Neisseria	
N. meningitidis	0.02
N. gonorrhoeae	0.05
Haemophilus influenzae	0.12
Pasteurella multocida	0.25
Branhamella catarrhalis	0.2
Proteus	
P. Vulgaris	64
P. mirabilis	128
Enterobacter	
E. cloacae	64
E. aerogenes	128
Escherichia coli	128
Klebsiella pneumoniae	128
Citrobacter freundii	128
Serratia marcescens	1600
Pseudomonas aeruginosa	6400
Morganella morganii	6400
ANAEROBIC BACTERIA	
Peptostreptococcus anaerobius	32
Clostridium	
C. sporogenes	32
C. difficile	32
Propionibacterium	
P. acnes	>128
P. granulosum	>128
P. avidum	>128
Peptococcus	
P. prevotii	>128
P. asaccharolyticus	>128
Bacteroides fragilis	>128

Effect of Inoculum Size

There is only a slight effect of inoculum size on BACTROBAN's minimum inhibitory concentrations (MIC's). For Staphylococcus aureus, inocula ranging from 10^6 cells/mL (undiluted) to 10 cells/mL (10^5 dilution) resulted in a two- to four-fold variation in the MIC values.

Effect of Composition and pH of Medium

The antibacterial activity of mupirocin was not influenced by the composition of the medium. The MIC values of mupirocin were generally two-to four-fold lower at acid pH (6.0) and two- to four-fold higher at alkaline pH (8.0) than those observed in the medium of normal pH (7.4).

Effect of Serum

Mupirocin was highly bound to serum protein (96.5% bound) and consequently, the activity of the compound was markedly reduced in the presence of human serum.

Minimum Bactericidal Concentrations

The MIC values of mupirocin against strains of Staphylococcus aureus ranged from 0.12 mcg/mL to 2.0 mcg/mL and the MBC values from 0.5 - >128 mcg/mL. In most cases, the MBC values were from eight- to thirty-two-fold higher than the corresponding MIC values.

Development of Resistance

The selection of mupirocin-resistant variants of Staphylococcus aureus after repeated exposure to increasing concentrations of the compound, occurred in a slow and stepwise fashion.

Cross-resistance to Other Antibiotics

There is no evidence of cross-resistance between mupirocin and other anti-microbial drugs.

PHARMACOLOGY

Percutaneous Absorption

In man, a mean topical dose of 0.487 grams of radiolabelled mupirocin in the ointment base applied directly to the skin resulted in less than 0.24% systemic availability of the applied dose up to 120 hours after application. The amount of mupirocin-related material in blood and plasma were less than approximately 1.2 ng/mL. The penetration of mupirocin into the outer layers of skin was a mean of 2.71% of the applied dose 24 hours after application. Assessment of the persistence of mupirocin, as measured microbiologically, after four days of twice daily application, showed no evidence of persistence 48 hours after the last dose. It is concluded that mupirocin itself does not form a depot in the skin. However, it is evident that metabolites (primarily, biologically inactive monic acid) of mupirocin are present in the skin for up to 168 hours after application.

Effect of Occlusion

In an in vitro study using normal cadaver skin, application of mupirocin with occlusion brought about a five-fold greater penetration of mupirocin than without occlusion, although the amount of penetration was still very low (up to 0.33%).

TOXICOLOGY

Acute Toxicology

The acute toxicity of mupirocin* was determined in mice and rats dosed orally, subcutaneously and intravenously.

* The dose level was in terms of pure sodium salt.

Acute Toxicity

Species	Route	Sex	LD_{50} (mg/kg)
Mice	Oral	M	> 5000
		F	> 5000
Rats	Oral	M	> 5000
		F	> 5000
Mice	s.c.	M	4000-5000
		F	4000-5000
Rats	s.c.	M	> 5000
		F	> 5000
Mice	i.v.	M	1638-2048
		F	1638-2048
Rats	i.v.	M	1310-2560
		F	1310-2560

All animals were observed for 14 days. Animals dosed orally remained in healthy condition throughout the study and there were no abnormal findings at post-mortem. Subcutaneously dosed animals showed injection site irritancy with scab formation. Mottled kidneys were found in all surviving mice and in half of those that did not survive. Animals dosed intravenously were observed to convulse immediately after dosing and sedation was evident in most animals. Mottled or pale kidneys were found in many of those surviving.

Subacute Toxicity

Rats:

Mupirocin was administered for 14 days to 3 groups of rats each comprising 10 males and 10 females. Two groups were subcutaneously (s.c.) dosed at 100 or 500 mg/kg/day and the third group was orally (p.o.) dosed at 100 mg/kg/day. A fourth and fifth group served as controls and the sixth group of 5 males and 5 females was the health screen. Clinical conditions and laboratory determinations were carried out. There were no treatment related deaths during the study. Injection site damage and alopecia was seen in all animals in the high subcutaneous dose group. Body weight gain, food consumption and water intake were unaffected by treatment. High s.c. dosed animals had slight decreases in haemoglobin, PCV (packed cell volume) and red cell count together with an increase in total leucocyte count and absolute neutrophil count. Orally dosed females had slightly increased haemoglobin and red cell counts and decreased MCV (mean corpuscular volume). Subcutaneously high dosed animals had reductions in SAP (serum alkaline phosphatase) activity, total protein, albumin A/G ratio together with increases in SGPT activity. The males also exhibited increased glucose and decreased potassium. Females receiving 500 mg/kg s.c. exhibited increased urine osmolality on day 13. Macroscopic examination revealed that there was a dose related increase in severity and extent of injection site irritancy. Increases in adrenal weights were noted in males from the high dose s.c. and orally dosed groups. The relative thymic weight in high dose s.c. males was reduced by 13% compared to controls. Significant increases of 31% and 20% were seen in the relative splenic weights of the male and female 500 mg/kg (s.c.) groups respectively and of 13% in the female oral dose group. Histological examination of the kidneys revealed minimal chronic inflammatory cell infiltration and was associated with occasional distended tubules and tubules characterised by the basophilic staining of the cells of the epithelium in the high dose s.c. and oral dose groups.

Squirrel Monkeys:

Mupirocin was administered to four groups of squirrel monkey each comprising of 2 males and 2 females. Two groups were dosed orally at 50 or 150 mg/kg/day for 14 days and two groups were dosed intramuscularly at 50 or 150 mg/kg/day for 14 days. A fifth group served as control. Clinical conditions and laboratory determinations were monitored and post-mortem and histopathologic determinations were carried out. There were no deaths during the study and no clinical adverse signs. Body weights and food intake were unaffected by treatment. Haematology, urinalysis and blood chemistry revealed no treatment-related effects. At post-mortem examinations, no effects of the

drug on organ weights was noted. Histopathological studies showed mild involution of the thymus in some treated animals. Examination of the injection site soft tissues of the i.m. dosed groups revealed mild to moderate irritation reactions.

Chronic Toxicity

Rats:

Mupirocin in a polyethylene glycol vehicle was applied topically to a shaved unabraded area on the dorsum of 3 groups of rats. Each group was comprised of 10 males and 10 females dosed at 10, 20 or 40 mg pfa/kg/day in dose volumes of 0.5 mL/kg, 1 mL/kg and 2 mL/kg respectively. Dosing was daily for 28 days. A fourth and fifth group served as control and vehicle control. Five male and five female rats were added to each of the control groups and the high dose groups to determine effect of drug withdrawal. At the end of the treatment period these three groups were left undosed for a period of two weeks before sacrificing. Clinical condition and laboratory determinations were monitored and post-mortem and histopathological determinations were carried out. In the final 4 days off-dose the high dose treated females gained less weight than those undosed controls (33%) and vehicle controls (20%). This was of uncertain significance. Blood chemistry showed slight decrease in glucose in the male intermediate dose group at day +29. Increases in glucose were noted in intermediate and high dose male groups and in increase in urine volume with decreased osmolality in the intermediate dose female group. Histological examination revealed vacuolation of parietal cells in females in all dose groups. This change was not observed in the high dose group after the off-dose period.

Rabbits:

Mupirocin in a cream base was applied topically to a shaved abraded area on the back of 3 groups of rabbits. Each group was comprised of 5 male and 5 female animals dosed at 10, 20 or 40 mg pfa/kg/day in dose volume of 0.5 mL/kg, 1 mL/kg and 2 mL/kg respectively. Treatment was daily for 30 days (6 hr/day under and occlusive dressing). A fourth and fifth group served as control and vehicle control. Two male and two female animals were added to each of the control groups and the high dose group to determine the effect of drug withdrawal. At the end of the treatment period these three groups were left undosed for a period of two weeks before sacrificing. Clinical conditions and laboratory determinations were monitored and post-mortem and histopathologic determinations were carried out. One male from the intermediate dose group died. Necropsy revealed a large abscess on the serosal surface of the colon. Similar body

weight gains were recorded for all groups throughout the study, however, marked increases in body weight gains were noted in all animals during off-dose period. Slight skin irritation (erythema, oedema and atonia) was noted in all treatment groups including vehicle control animals. Macroscopic pathology revealed minimal acanthosis of the epidermis and/or leucocyte accumulation in the statum corneum.

Rats:

Mupirocin was administered daily by the subcutaneous route to 3 groups of rats each comprising 15 males and 15 females at doses of 10, 40 or 100 mg/kg/day for 3 months. A fourth group (control) received sterile saline. Five male and 5 female rats were added to each of the high dose and control groups to determine the effect of drug withdrawal. At the end of the treatment period, these two groups were left undosed for 28 days. Clinical conditions and laboratory determinations were monitored and post-mortem and histopathological determinations were carried out. One female was killed in extremis on day 3 and replaced. Autopsy revealed no treatment related causes. One low dose female and one intermediate dose male died under anaesthetic and a further female was killed in extremis following accidental injury. Alopecia and scab formation was seen at the injection sites of high dose males from day 7 onward. Mild signs of sialodacryoadenitis were noted in all groups from day 42. Weight gain in high dose females was reduced after 6 weeks of dosing but was comparable to control by the end of dosing period. In intermediate dose males, weight gain was 14% overall greater than controls. Low dose females gained 63% more than controls in the final 5 weeks of dosing. Food intake was greater in intermediate dose males. Water intake of males increased during week four.

Female rats had decreased water consumption in week 4 but low doe females had significant increase in week 12. During "off-dose", females in the high dose group had slightly less water consumption than controls. There were no significant haematologic changes except for a slight reduction in red cell parameters in treated females at the interim examination. Increases in ALT (alanine amino-transferase) were noted intermediate and high dose males. Decreased total protein and albumin in high dose males and increased A/G ratio in low dose males was also noted. Increases in urine volume occurred in high dose males and females. Macroscopic examinations revealed a treatment related incidence of injection site irritation. After treatment period, there was an increase in spleen weight in the high dose females. A significant increase in liver weights of high dose level females at this time showed reversal upon drug withdrawal.

Dogs:

A similar study was carried out in beagle dogs. Mupirocin was administered daily by the route to 3 groups of dogs each comprising 4 males and 4 females at doses of 5, 10 and 20 mg/kg/day. (These doses were reduced from 10, 40 and 80 mg/kg respectively on day 4). A fourth group (control) received sterile saline. Two males and two females were added to each of the high dose and control groups to determine the effect of drug withdrawal. At the end of the treatment period, these two groups were left undosed for a period of 28 days. Immediate reaction to treatment in the form of muscular weakness and convulsions was evident in several dogs at levels of 40 and 80 mg/kg. On lowering of these dose levels, reactions continued until day 6 until a reduced injection rate was introduced. There were no mortalities. A decrease in total leucocyte count was seen in most intermediate and high dose males and most females in all dose groups. Blood chemistry revealed increases in A/G ratios in 4 high dose males at terminal examination. Analysis of ECG's from dogs showing adverse reactions at onset of dosing showed pronounced bradycardia, sometimes with tachycardia with onset, during or immediately after dosing and recovery within 2 minutes. Macroscopic, pathologic and histopathologic examinations revealed no changes considered to be related to treatment.

Reproductive studies

Fertility and General Reproductive performance:

Mupirocin was administered subcutaneously to 3 groups of rats, each comprising 28 males and 28 females, at doses of 10, 40 and 100 mg/kg/day. A fourth group (control) received the vehicle (sterile saline). Male rats were dosed daily from 10 weeks prior to mating until successful littering by F_0 females. Female rats were treated daily from day 15 prior to mating until day 24 post-partum or until selected for caesarean section on gestation day 21. On gestation day 21, 14 females/group were sacrificed and a caesarean section carried out and the remaining 14/group were allowed to litter normally. From these litters a total of 28 males and 28 females were selected to form the F_1 generation. They were mated at 11 weeks of age and the procedures followed were comparable to F_0 generation. One female animal in the high dose group was killed, not due to a direct effect of treatment. Alopecia and scabbing at injection sites was seen in the female intermediate dose group and in all animals at the high dose level. Top dose females had a reduction in body weight gains latter part of gestation. Fertility and general reproductive performance were not affected by treatment. In the litters of females sacrificed for caesarean section there were treatment related trends in reduction in general cranial

ossification. Pups from females allowed to litter were unaffected by parental treatment. The F_1 generation showed no signs of physical condition ascribable to treatment of the F_0 generation. One female in the low dose group was killed following total litter loss on day 2 post-partum. Before pairing females derived from treated parents showed significant increases in body weight gains compared to animals from control parents. The rate was similar in all groups during gestation but significantly reduced in the intermediate and high dose group animals during lactation. Males derived from high dose F_0 generation had slightly poorer recall ability. In the F_1 animals allowed to litter the only effect recorded in the pups was a significant reduction in the percentage of females in the top dose group to have developed the static righting reflex.

Teratology

Three groups of 15 female rabbits were mated and mupirocin was then subcutaneously administered from day 6 to day 18 of gestation at doses of 10, 40 and 160 mg/kg/day. A fourth group (control) was dosed with physiological saline (vehicle). On day 29 of gestation, the animals were sacrificed and caesarean section carried out. Orange colouration of the urine was seen in the majority of high dose animals and in some intermediate dose animals. Four high dose animals showed palpable thickening and tightening of the skin and associated abnormal gait. Three of these affected animals aborted and were killed before day 29. One other animal in the high dose group and one in the control group also aborted but survived until termination of study. Higher incidence of anorexia and reduced fecal output during dosing or post-dosing periods was noticed in the intermediate and high dose groups. Maternal weight gain was impaired in the high dose groups. Maternal weight gain was impaired in the high dose group. A slightly lower mean number of corpora lutea was recorded in all test groups and pre-implantation loss was higher in low and intermediate dose groups resulting in lower number of implantations but these were not statistically significant. Autopsy of high dose animals revealed dose-related injection site reactions with subcutaneous haemorrhage, dermal thickening and subcutaneous white discolouration in the dorsal area. There were no significant changes in litter parameters and incidences of major malformations, minor anomalies and skeletal variants were unaffected by treatment.

Perinatal and Postnatal Studies

Mupirocin was administered subcutaneously to 3 groups, each comprising 22 pre-mated rats, at doses of 11.1, 44.2 or 106.7 mg/kg/day from day 15 of gestation to day 25 post-partum. A fourth group (control) was dosed with sterile saline. One parent animal in the

low dose group was killed following extreme dystocia. Local irritancy in the form of swelling and/or scabbing at the injection site was seen in all doe levels. Pregnancy rate and implantation index and length of gestation was comparable for all groups. Autopsy of parent animals revealed an increased number of injection site reactions in the form of subdermal haemorrhaging, scabbing and alopecia in the high dose group. These incidences were less severe in the low and intermediate dose groups. There was no evidence of treatment related effect on the general condition of the offspring. Group mean litter size was slightly lower than control in the intermediate dose group and markedly lower in the higher dose group. There was a slight reduction in the viability index (at day 4) of the high dose animals with more minimal effects seen in the remaining treated and control groups. The F_1 generation parameters revealed no other meaningful differences or dose related trends in litter observations, behavioural and developmental indices.

Irritation and Sensitization Studies

Animal

Rabbits:

The area on the back of six female rabbits was clipped free from hair. The left side was left intact, the right side was abraded, penetrating the stratum corneum but no damaging the underlying dermis. Mupirocin in an ointment base was then applied to both sides at a dose of 0.5mL and covered with gauze for a period of 24 hours. Dressings were then removed and skin wiped free of ointment. Observations made at 24 hours and 72 hours after treatment revealed no adverse skin reactions.

Guinea Pigs:

An area on either side of the trunk of 50 male guinea pigs was clipped free of hair and groups were dosed as follows:

Group 1, comprised of 20 animals was dosed with 0.5 mL mupirocin in a polyethylene glycol base.

Group 2, control was comprised of 20 animals and dosed with 0.5 mL base formulation.

Group 3, positive control was comprised of 10 animals and dosed with 0.5 mL DNCB (0.1% W/V 1-chloro-2,4-dinitrobenzene).

Each group was dosed a total of 10 times, each 3 days apart at a different skin site. Fourteen days after the last dose, each group received a challenge application. Skin reactions were assessed 24 hours and 48 hours after each induction and challenge application. Skin reactions were assessed 24 and 48 hours after each induction and

challenge application. One animal in group 1 was killed on day 6 following a prolapse and another animal died on day 18. No abnormalities were noted at necropsy. One control animal died on day 24. No abnormalities were noted at necropsy. No adverse skin reactions were noted in any of the control groups during the induction period. Twenty-four hours following the challenge application, five animals in group 1 showed very slight erythema. This had disappeared in all but 1 of the animals at the 48 hour observation. Following the challenge application in group 3, all animals produced skin responses in the form of slight to well-defined erythema and slight oedema. These responses were increased slightly at the 48 hour observation.

Human:

Mupirocin in a polyethylene glycol base was applied to the arms of 80 volunteers 2 or 3 times daily for 21 or 28 days at doses of approximately 1 mL per application on a site 5 cm X 5 cm. A further 19 subjects applied the base only in the same manner. After 7 or 14 days without treatment, a rechallenge was made with another similar application. Haematology, clinical chemistry, urinalysis and any reactions to the applications were monitored throughout the study. One subject receiving active drug demonstrated slight redness at the application site on day 2. Another subject developed a rash over the dosing site 18 days after the rechallenge. This was not considered an allergic response to the application. There were no drug related changes in clinical chemistry, haematology or urinalysis.

Mupirocin in a polyethylene glycol base was applied to the arms of 107 volunteers twice daily for 28 days at doses of 0.1 mL/application to a site 5 cm X 5 cm. The site was then covered with an occlusive dressing. the application sites were exposed to air up to 1 hour/day. A further 16 subjects received the base only in a similar manner. Seven to 14 days after dosing, a patch sensitization test was carried out, leaving the patch in place for 48 hours. Hematology, clinical chemistry, urinalysis and any reactions to dosing were regularly monitored for the duration of the study. One subject receiving active material withdrew from the study because of pruritis under the occlusive dressing. A number of subjects experienced itching related to the occlusive dressing. Eight subjects receiving active material developed transient rashes at the application sites, however, 5/8 had not removed the occlusion daily. five subjects experienced burning, itching or aching pains in association with the application but without cutaneous rashes. The patch sensitization test did not result in a reaction to the application. There were no drug related changes in haematology, clinical chemistry or urinalysis parameters.

Seventy-eight subjects who had received mupirocin in the previous 1 1/2 - 35 months participated in a rechallenge test. Each subject had 0.1 mL of 2% mupirocin ointment applied to an "A1-test" disc, placed on the arm and occluded for 48 hours. None of these subjects showed evidence of sensitization.

Twenty-five volunteers had 2% mupirocin ointment applied to sites on their forearms, which had been previously treated with 1.0% sodium lauryl sulphate. Each subject was treated with 0.3 grams for five 48 hour periods. Ten days later a challenge application was applied to a different site which had been pre-treated with 10.0% aqueous solution of sodium lauryl sulphate. There were no instances of irritation or contact sensitization during the application period or after challenge with either material.

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